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Policy Number: C9674-A

Enzyme Replacement Therapy for Gaucher Disease (Cerezyme, Elelyso, Vpriv)

PRODUCTS AFFECTED

Cerezyme (imiglucerase), Elelyso (taliglucerase alfa), Vpriv (velaglucerase alfa)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Type 1 Gaucher disease, Type 3 Gaucher Disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. TYPE 1 GAUCHER DISEASE (GD):
   1. Documented diagnosis of Type 1 Gaucher Disease (GD)
      AND

2. Documentation diagnosis was confirmed by Glucocerebrosidase activity in the white blood cells or skin fibroblasts less than or equal to 30% of normal activity OR Genotype testing indicating a mutation of two alleles of the glucocerebrosidase genome [DOCUMENTATION REQUIRED]
   AND
3. The requested drug will be used as monotherapy and is NOT to be used concurrently with other medications for GD [i.e., Cerezyme, VPRIV, Elelyso, Cerdelga, or Zavesca]
   AND
4. Documentation of member's therapeutic goals based on their individual baseline symptoms (e.g., bone pain, fatigue, dyspnea, angina, abdominal distension), overall health, and quality of life
   AND
5. FOR ADULT MEMBERS (≥ 18 YEARS OF AGE): Documentation of member experiencing any of the following signs/symptoms indicating severe manifestations where enzyme replacement therapy (ERT) is recommended: splenomegaly, anemia, thrombocytopenia, diffuse bone pain vertebral compression fractures, fragility fractures, interstitial lung disease, elevated basal metabolic rate, insulin resistance, lipid abnormalities, hepatic or splenic infarcts, hepatitis, portal hypertension, hepatomegaly, avascular necrosis, or lytic disease
   OR
   FOR PEDIATRIC MEMBERS: Documentation of member experiencing any of the following signs/symptoms indicating ERT is recommended: Evidence of skeletal involvement, Hepatosplenomegaly, Growth failure secondary to GD and not associated with other conditions, Symptomatic disease, including abdominal or bone pain, fatigue, exertional limitation, weakness, or cachexia, Anemia or Platelet count less than 60,000 per mm3 or documented abnormal bleeding episode(s)

B. TYPE 3 (NEURONOPATHIC) GAUCHER DISEASE:

1. Documented diagnosis of neuronopathic Type 3 Gaucher Disease (GD)
   AND
2. Documentation diagnosis was confirmed by Glucocerebrosidase activity in the white blood cells or skin fibroblasts less than or equal to 30% of normal activity OR Genotype testing indicating the presence of TWO or more alleles for neuropathic GD [DOCUMENTATION REQUIRED]
   AND
3. Documentation of member experiencing neurologic manifestations consistent with Type 3 GD (e.g., abnormal eye movement, encephalopathy, ophthalmoplegia, seizures, progressive myoclonic epilepsy, cerebellar ataxia or spasticity, dementia) OR Documentation of SEVERE visceral symptoms such as kyphoscoliosis and barreled chest.
   AND
4. Documentation of member baseline non-neurologic signs/symptoms (e.g., splenomegaly, hepatomegaly, anemia, thrombocytopenia, skeletal abnormalities)
   NOTE: ERT does not cross the blood-brain barrier and therefore has limited ability to impact the CNS manifestation of the disease. However, non-neurologic signs and symptoms do respond to ERT.
   AND
5. The requested drug will be used as monotherapy and is NOT to be used concurrently with other medications for GD [i.e., Cerezyme, VPRIV, Elelyso]

CONTINUATION OF THERAPY:

B. TYPE 1 GAUCHER DISEASE:

1. Documentation of disease response as indicated by one or more of the following (compared to pre-treatment baseline): Improvement in symptoms (e.g., bone pain, fatigue, dyspnea, angina, abdominal distension, diminished quality of life, etc.), reduction in size of liver or spleen, improvement in hemoglobin/anemia, improvement in skeletal disease, improvement in platelet counts
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., serious hypersensitivity reactions, including anaphylaxis)

C. TYPE 3 GAUCHER DISEASE:

1. Documentation of disease response as indicated by improvement in or stabilization of neurologic manifestations of disease, reduction in size of liver or spleen, improvement in hemoglobin/anemia, improvement in skeletal disease, improvement in platelet counts
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., serious hypersensitivity reactions, including anaphylaxis)

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified geneticist, pediatric metabolic specialist, hematologist, or physician experienced in the management of Gaucher Disease. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
Cerezyme (imiglucerase): 2 years of age and older
Elelyso (taliglucerase alfa) and VPRIV (velaglucerase alfa): 4 years of age or older

QUANTITY:
Cerezyme: Maximum 60 units/kg once every 2 weeks (see Appendix)
Elelyso: Maximum 60 units/kg every other week
Vpriv: Maximum 60 units/kg every other week

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Cerezyme (imiglucerase), Elelyso (taliglucerase alfa), Vpriv (velaglucerase alfa). For information on site of care, see:
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Agents for Gaucher Disease

FDA-APPROVED USES:
Cerezyme (imiglucerase): Indicated for treatment of adults and pediatric patients 2 years of age and older with Type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly

Elelyso (taliglucerase): Indicated for the treatment of patients 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease

Vpriv (velaglucerase alfa): Indicated for long-term enzyme replacement therapy (ERT) for patients with Type 1 Gaucher disease

E75.22 Gaucher disease

COMPENDIAL APPROVED OFF-LABELED USES:

Type 3 (neuronopathic) Gaucher disease

APPENDIX

APPENDIX:

The recommended dosage of Cerezyme based upon disease severity ranges from 2.5 units/kg three times a week to 60 units/kg once every two weeks. Titrate the dosage based on clinical manifestations of disease and therapeutic goals for the patient.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Gaucher Disease (GD)

A rare, autosomal recessive, lysosomal storage disorder caused by mutations in the glucocerebrosidase gene, resulting in the accumulation of glucosylceramide in macrophage cells. Characterized by hepatosplenomegaly, thrombocytopenia and anemia, and is significantly more common among persons of Ashkenazi Jewish descent, classified into 3 clinical forms of GD defined by absence or presence and progression of neurologic involvement. The highly variable presentation of GD depends not only on the disease severity, organ involvement, and progression rates but on the type or subtype:

Type 1 (non-neuronopathic form): bone disease and lack of primary central nervous system involvement

Type 2 (acute neuronopathic form): severe neurologic impairment without bone involvement

Type 3 (chronic or subacute neuronopathic form): neurologic impairment and bone disease subtype fetal or perinatal-lethal form: death in utero or shortly after birth, subtype cardiovascular form: cardiovascular disease such as calcification of the mitral and aortic valves

Type 1 carries the best prognosis with the longest life expectancy

Management of GD

The primary goals of therapy are elimination or improvement of symptoms, prevention of irreversible damage, and improvement in the overall health and quality of life. An additional goal in pediatric patients is optimization of growth.

Treatment of GD consists of therapy two mechanisms: replacing the missing or defective glucosylcerebrosidase with a genetically engineered enzyme (ERT), or reducing the synthesis of the glucosylceramide (SRT). SRT differs from ERT as it does not attempt to replace absent or impaired enzyme function; instead, SRT interrupts the function of glucosylceramide synthase, an enzyme responsible for the production of glucosylceramide, the substance that accumulates in the body and results in symptoms of GD

1) Enzyme Replacement Therapy (ERT): ERTs act by supplementing glucocerebrosidase, the enzyme that breaks down glucosylceramide. ERT therapies currently available: Cerezyme (imiglucerase), VPRIV (velaglucerase alfa), and Elelyso (taliglucerase alfa). ERT is currently the standard of care for treatment and is used in symptomatic patients. The goal of ERT is to provide the appropriate amount of enzyme to allow excess material to be degraded. ERT works by supplementing or replacing the patient's missing or deficient enzyme. Because ERT does not cross the blood brain barrier, it does not address conditions or symptoms related to the central nervous system in Types 2 and 3 GD.
2) Substrate Reduction Therapy (SRT): SRT aims to restore metabolic homeostasis by limiting the amount of substrate precursor synthesized (and eventually subject to catabolism) to a level that can be effectively cleared by the mutant enzyme with residual hydrolytic activity. The goal of SRT is to minimize the amount of production and accumulation of excess material, or a particular substrate (glucosylceramide or GL1), within cells. SRT works by reducing the amount of GL1 that a cell makes. This means that even though patients with GD are deficient in an enzyme that breaks

down GL1, with SRT, the enzyme they do have is better able to prevent GL1 from accumulating inside cells.

The two SRT therapies are Zavesca (miglustat) and Cerdelga. Zavesca (miglustat) is only indicated in patients with mild or moderate disease who are unable to tolerate or take ERT.

Therefore, it is reserved as a last line option. Both SRT regimens are administered orally. The policy addresses the use of substrate reduction therapy (SRT), Zavesca (miglustat).

Management of Gaucher disease depends on type and clinical presentation. In symptomatic patients with Type 1 Gaucher disease, treatment consists of intravenous ERT or oral SRT

- ERT with imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), or taliglucerase alfa (Elelyso) is primary treatment

SRT, miglustat, may be used as second-line therapy for adults unable to take ERT

The decision to offer Gaucher-specific therapy (enzyme-replacement therapy [ERT] or substrate- reduction therapy [SRT]) in patients with non-neuronopathic GD (type 1 Gaucher disease [GD1]) is based upon disease severity, as determined by the initial assessment, or significant disease progression, as demonstrated through regular follow-up. ERT with a recombinant glucocerebrosidase (imiglucerase, velaglucerase alfa, or taliglucerase alpha) or SRT with eliglustat are the preferred treatments for patients with clinically significant manifestations of non- neuronopathic GD (GD1). (Hughes, D. 2018)

ERT with imiglucerase or velaglucerase (off-label use) is also an option in patients with chronic neuronopathic GD (type 3 [GD3]) who have visceral manifestations and in patients at risk for GD3, but it is not suitable for patients with acute neuronopathic GD (type 2 [GD2]). (Hughes, D. 2018) International Collaborative Gaucher Group (ICGG); US Regional Coordinators

All children with GD treated with ERT since pediatric patients are at high-risk for irreversible, morbid complications according to the ICGG. The diagnosis of GD in the first and second decades of life is indicative of a rapidly progressive course; therefore early intervention is necessary for these children, during the time when the skeleton is immature, to enable them to attain their peak skeletal mass by early adulthood.

Comprehensive recommendations for the initial assessment and monitoring of individuals with type 1 and type 3 GD was published by the ICGG. These recommendations take into consideration the multiple variables that need to be addressed, including the hematologic, visceral, bone, and neurological aspects of the disease. Additionally, these recommendations provide guidance for the timing of the various tests required. (Weinreb NJ, et al. 2004)

Revised Recommendations for the Treatment of Gaucher Disease (GD) in Children

Kaplan et al. (2013) published updated recommendations for the management of children with GD. According to the Gaucher Registry, children treated with alglucerase or imiglucerase demonstrated most of the hematologic benefits and approximately half of the organomegaly benefits during the first year of treatment, with continued or sustained improvement in all parameters for greater than or equal to 8 years of treatment. ERT was recommended for all symptomatic children with type 1 and 3 GD, which can prevent debilitating and often irreversible disease progression and allow those with non- neuropathic disease to lead normal healthy lives.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Enzyme Replacement Therapy (ERT) for Gaucher Disease [Cerezyme (imiglucerase); Elelyso (taliglucerase alfa); Vpriv (velaglucerase alfa)] are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to ERT include: No labeled contraindications for any agent in this policy.

OTHER SPECIAL CONSIDERATIONS:

Elelyso (taliglucerase alfa) and Vpriv (velaglucerase alfa) have a Black Box Warning for hypersensitivity reactions including anaphylaxis.

Pregnancy considerations: Based on available information, an increased risk of adverse pregnancy outcomes

has not been observed following maternal use of velaglucerase alfa (Elstein 2014; Lau 2018). Available data on more than 500 pregnancies from the international Gaucher Disease registry, post marketing reports, published observational studies and case reports with Cerezyme or non–US-licensed imiglucerase use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. The limited available data on ELELYSO use in pregnant women are not sufficient to inform a drug-associated risk. Pregnancy may exacerbate existing type I Gaucher disease or result in new symptoms. Women with type I Gaucher disease have an increased risk of spontaneous abortion if disease is not well controlled. Adverse pregnancy outcomes, including hepatosplenomegaly and thrombocytopenia, may occur.

Antibody formation
The development of IgG antibodies has been reported; the clinical significance is unknown. Patients with an immune response to other enzyme replacement therapies who are switching to velaglucerase alfa should be monitored for antibody development.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J1786	Injection, imiglucerase, 10 units
J3060	Injection, taliglucerase alfa, 10 units
J3385	Injection, velaglucerase alfa, 100 units

AVAILABLE DOSAGE FORMS:
Cerezyme SOLR 400UNIT single-dose vial
Elelyso SOLR 200UNIT single-dose vial
Vpriv SOLR 400UNIT single-dose vial

REFERENCES

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2. Elelyso (taliglucerase alfa) for injection, for intravenous use [prescribing information]. New York, NY; Pfizer Inc; January 2025.
3. Vpriv (velaglucerase alfa) for injection, for intravenous use [prescribing information]. Lexington, MA: Shire Human Genetic Therapies; September 2024.
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12. Martins AM, Valadares ER, Porta G, et al. Recommendations on diagnosis, treatment, and monitoring for Gaucher disease. J Pediatr. 2009 Oct;155(4 Suppl):S10-8.
13. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. Eur J Pediatr. 2013 Apr;172(4):447-58: doi: 10.1007/s00431- 012- 1771-z. Epub 2012 Jul 8

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Coding/Billing Information References	Q3 2025
REVISION- Notable revisions: Required Medical Information Quantity Appendix Other Special Considerations Available Dosage Forms References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Quantity FDA-Approved Uses Compendial Approved Off-Labeled Uses Appendix Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q3 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Prescriber Requirements Quantity Contraindications/Exclusions/Discontinuation References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file